Medical Hypotheses 21: 421-430, 1986

UNMASKING AIDS: CHEMICAL IMMUNOSUPPRESSION AND SERONEGATIVE SYPHILIS

J.J. McKenna, R. Miles, D. Lemen, S.A. Dunford and R. Renirie, Institute For Thermobaric Studies, 2811 Martin Luther King, Jr. Way, Berkeley, California 94703.

ABSTRACT

In both African AIDS populations and homosexual populations outside of Africa, a high incidence of syphilis and multiple exposures to infectious diseases results in frequent, often abusive use of antibiotics. Epidemiological evidence exists for chemical immunosuppression resulting from antibiotics and other prescribed and recreational drugs prior to the current AIDS crisis.

Analysis and review of literature is given on the effects of subcurative doses of antibiotics masking and distorting the expression of secondary and tertiary syphilis. A high incidence of seronegative syphilis is found in Africa and compares with Western reports of seronegativity and persistence of treponemes despite adequate antibiotic therapies. Late latent and tertiary syphilis produce symptoms and immunosuppression comparable to that seen in the current AIDS crisis.

Screening procedures instituted for a group of gay men with AIDS and AIDS related conditions is revealing evidence of chemically immunosuppressed syphilis as a factor in AIDS.

Key words: AIDS, immunosuppression, syphilis, chemical immunosuppression, seronegativity, immunosuppressive sera, etiology of AIDS.

INTRODUCTION

Historically, acquired immune deficiency syndromes occur in patients with conditions of debilitation, malnourishment, drug immunosuppression or chronic diseases, particularly those of the liver and kidneys, and under the complex conditions of organ transplants.

Acquired immune suppression is the rationale used to explain the susceptibility of certain patients to opportunistic infections--certain fungi, viruses, parasites, bacteria--that are endemic but ordinarily held in check by the immune system.

In the current AIDS crisis, this rationale has been modified by the assumption that the HTLV-III (or other virus) invades the immune system of an otherwise healthy body, hence proposing a new etiology for acquired immune deficiency syndromes. (1-4)

Preliminary surveys indicated a history of multiple and chronic systemic insults, disproportionately high use of antibiotics and other immunosuppressive drugs, high incidence of "recreational" or street drugs, and multiple presentations of chronic inflammation and irritation during the 10 years prior to our survey. It is our hypothesis that a prior history of chronic inflammation combined with antibiotic and other immunosuppressive drugs created an environment in which a wide array of microorganisms could grow and reproduce. Essentially, a "hothouse" effect arising from the life style, drug use patterns and disease exposures are the conditions we see as necessary for an acquired immune deficiency syndrome.

Following our February-April 1985 survey of histories of immunosuppression in the gay community, we undertook additional surveys, obtaining detailed medical and personal histories of 100 men. Of this group 24 were AIDS diagnosed. The remainder were identified with AIDS-related conditions, or at high risk for an ARC diagnosis according to CDC guidelines used by their physicians. Many had been or were sexual partners of men known to have AIDS or ARC.

What emerged from this data was a profile substantiating disproportionate antibiotic and immunosuppressive drug use. Drugs which have known myelotoxic effects or which adversely affected liver and kidney functions according to the Physicians' Desk Reference and the Lippincott Drug Facts and Comparisons are considered immunosuppressive.

Among the most common presentations we have found are the following:

Gonorrhea: multiple incidents with treatment by antibiotic therapies; twenty incidents per year for two or more years is not uncommon.
Hepatitis: high incidence of known hepatitis or positive antigen tests; 10% had chronic hepatitis of five years or longer duration.
Non-specific urethritis: multiple presentations, sometimes chronic in that an individual will report 6 or 7 episodes per year for up to 8 years; higher doses and longer duration of antibiotics as the condition became resistant to chemical intervention.
Dermatological eruptions: specific, palliative and prophylactic use of antibiotics, tetracycline, and corticosteroids for skin eruptions; reports of prescribed tetracycline for 5 to 18 years continuously.
Sedatives, tranquilizers, and mood drugs: for psychological conditions; prescribed or used without prescription.
Chronic sore throat: More than 50% report frequent episodes with antibiotic medications.
Herpes simplex: 25% report chronic herpes; 90% herpes in the past 10 years.
Allergies: high incidence of history of chronic and severe allergies, allergy medications, and symptomatic suppressants.
Lymphadenopathy: frequent to chronic swollen lymph nodes in 40% of sample for up to 25 years preceding survey.
Diarrhea: high incidence of known and unknown etiologies; frequent parasites suspected, and parasitic treatments with and without confirmation of actual organisms in nearly 30% of our study.
Alcohol: Nearly universal use of alcohol on a daily basis for years. Moderation of use during the last four to six years; prior use considered excessive in the majority of cases.
Recreational drugs: nearly universal use of marijuana; a multiple and complex use of LSD, MDA, PCP, heroin, cocaine, amyl and butyl nitrates, amphetamines, barbiturates, ethyl chloride, opium, mushrooms, and what are referred to as "designer drugs" where the specific molecular structure has been modified to slightly alter an illegal compound to avoid prosecution if the producer or the dealers and users are found with the drugs and

arrested. Prosecution is confounded because the drug is not specifically the "illegal" drug, but the effects of these altered compounds are not known.

Approximately one-fourth of our sample shared 9 or more of the conditions and patterns described above. That is, the presentations of those disorders and both the prescribed and recreational drug use are concentrated in this discrete sub-set of the surveyed population.

ALL INDIVIDUALS WHO HAD BEEN DIAGNOSED AS HAVING AIDS OR ARC WERE FOUND TO BE IN THIS SUB-SET OF THE GAY POPULATIONS SURVEYED.

Therefore, we initially concluded that the history of immunosuppressive drug use, both prescribed and recreational, and the profile of chronic systemic inflammation presented by these histories had created an ideal condition for diverse micro-organisms to proliferate--the Acquired Immune Deficiency Syndrome.

From the perspective of this hypothesis, the retrovirus found in AIDS and ARC diagnosed individuals could be a co-factor, not necessarily a new etiology, further stressing an already compromised system and being itself yet another opportunistic micro-organism in a chemically immunosuppressed system.

In May 1985 we began detoxification and rehabilitation programs to educate the gay community concerning those factors of life style, diet, stress management, behavior, drug use, etc. that would shift individuals out of the pattern of chronic inflammation into a more normal physiological thermodynamic. Our program goal in working with the gay community is to identify and alter those patterns contributing to the traditional acquired immune deficiency profile found in each man's history.

Recent reports (6) indicate that 79% of all AIDS cases are considered drug abusers. While interpretations of "drug abuse" focus on street drugs, our studies confirm previously reported high and more frequent use of <u>prescription drugs</u> in the homosexual population. (1-4, 44-50) What is overlooked are the possible ramifications of antibiotic or other drug-induced immune suppression in a sexually active population at high risk for sexually transmitted diseases.

The distortions in disease presentation, serology, diagnosis, treatment, and prognosis for chemically suppressed or inadequately treated venereal disease are not easily recognized. Misdiagnosis and failure to consider chemical immunosuppression of venereal disease, specifically syphilis, can generate bizarre and baffling symptoms that are remarkably consistent with AIDS presentations in the homosexual community.

In our continuing research effort, a review of reference works of pre-1977 publications (6-10) revealed dramatic differences in the disease presentations of Kaposi's sarcoma and the post-1977 presentations of Kaposi's sarcoma in the gay community and in the presentations of our program participants. (77-80)

In the literature of the early 1950s there were only scattered reports of significant clusters of children dying from pneumocystis (69-72; 75), and those were in hospital deaths where other diseases and use of antibiotics were involved. Adults contracting pneumocystis had rare fatalities (68, 73, 74, 76). Men in the armed forces were known to recover in three weeks to three months without complication (74, 76).

Pneumocystis was originally clustered with a variety of non-bacterial forms of pneumonia under the general categories of primary atypical pneumonia and infiltrating interstitial

pneumonia. (67-72) Included in this literature were references to syphilitic or white pneumonia as being part of the infiltrating interstitial pneumonias (68, 74, 76), and a primary atypical pneumonia developing in men who had syphilis or who were being treated for syphilis (23-29, 76). While these presentations were consistent with pneumocystis, syphilis did not have the ease of resolution in both congenital and adult presentations.

Syphilis has been mistaken for AIDS (11), for neoplasms (12,14, 20), for nephritis (15-17), dementia (12-14, 45, 46), for lymphomas (19-21, 33), psoriasis and other dermatological configurations (12-14, 29-32). Lymphadenopathy, sore throat, malaise, fever, flu-like symptoms, headache, meningismus, musculo-skeletal aches, hoarseness, loss of appetite and weight loss are all common symptoms of secondary syphilis (12, 13), and AIDS (1-4).

Cutaneous lesions in secondary syphilis are generally macular, roseolar, papular, papulo-squamous or pustular. Morphological features of the lesions tend to vary with the duration of the eruption. Vegetative hypertrophies of late syphilis, called condylomata lata, may be raised, slightly lobulated or smooth papules. Cutaneous lesions of secondary syphilis sometimes leave hyper or hypopigmentation (11-14, 30, 32). Hair loss, visceral lesions, hepatitis, glomerulonephritis, myositis, auditory neuritis, syphilitic labyrinthitis, and symptomatic neurosyphilis have all been reported (11-14).

Purple lesions on the ear lobe (30), infiltrating interstitial pneumonia of the lungs (23-29), gummata of the lungs (27, 28), sarcoid-like granulomas (18, 81), varioliform and framboesiform facial lesions (30-32) show remarkable similarity in histopathology and symptomology with Kaposi's sarcoma (67, 77-80) as it has come to be seen in the gay epidemic of AIDS.

African incidence of AIDS is highest in those areas of Africa where syphilis is epidemic. Given the known high incidence of syphilis in gay communities (11, 22, 34-38) as well, there needs to be consideration of a possible high incidence of undetected syphilis in the current discussion of AIDS etiology.

In Africa, the prevalence of venereal syphilis is considerably higher than in Europe and the U.S.A. Reliable statistics are generally confined to hospital patients and selected population groups. However, the effects on symptoms of casual and abusive antibiotic use and false negative serology are better recognized than in Western countries. (45-47)

Reports from Uganda indicate false negative serology creates severe problems in diagnosis of secondary syphilis either because of the occurrence of a non-specific reaction or no reaction at all. In one study, 3.3% of cases with secondary syphilis and almost half of those with GPI (general paresis of the insane) were non-reactive. In terms of titres, more than 79% of cases with GPI (attributed to tertiary neurosyphilis), more than 60% of cases of primary syphilis and more than 10% of cases of secondary syphilis were reactive at 1:4 or less. Using the same tests, it was shown that only one out of 69 Finnish patients with secondary syphilis had a VDRL slide titre as low as 1:4 (45). In this same study, the FTA-ABS test was reactive in only 86 out of 129 patients with primary syphilis (67%), in all those with secondary, latent and congenital syphilis, in 97.5% of those with tertiary syphilis, and in 36% of the 99 patients with genital sores.

While articles on syphilis warn against false positive results from serological testing, physicians have been relatively uninformed about false negative reactions, particularly in individuals who have been treated with sub-curative doses of penicillin or other antibiotics for other disorders. Recent articles on the complete effectiveness of penicillin ignore a significant body of literature alerting the physician to the suppression of

primary syphilis symptoms and the induction of a seronegativity consistent with secondary, latent and tertiary syphilis. (39-59)

Since its introduction in the treatment of syphilis in the late 1940s, subcurative doses of penicillin have been recognized as having a masking effect on primary symptoms of syphilis. This forces a latent stage with often bizarre symptoms eventually emerging. Seropositive confirmation is available in only 60 to 70% of the cases (55-59).

Failure of serological tests to accurately identify disease status raises serious questions of treatment evaluation. Penicillin is effective against treponemes only as they are reproducing (39-42, 52, 54, 56, 57). During a chemically induced latency, a slower incubation may make the usual antisyphilitic treatment ineffective.

Inherent in laboratory testing for serological response is the assumption that the immune system is competent to respond and produce the antibody. There is the further assumption that once produced, the antibody will always be present.

While AIDS patients may produce antibodies, even overproduce certain antibodies, the first assumption concerning competence cannot be considered unquestionably valid in conditions of recognizable immunosuppression, regardless of the cause of the suppression. Nor can the second assumption of persistence of antibodies be proven in all cases. Individuals with severe immune suppression may not produce antibodies; they may produce erratically, abnormally or superabundantly. A system overwhelmed with antigens may produce a general suppression of cell-mediated immunity. Or a system that has eliminated the micro-organism specific to the antigen may cease to produce antigens and specific antibodies. Or successive damage to chemistry and function may alter the expected response, weakening or deranging the biochemical markers. Or a changed chemical environment may have mutated the treponemes.

While reagin tests for syphilis may vary in reactivity, most physicians assume that the FTA-ABS is always positive once syphilis has presented, and that it remains positive for life. This is a fallacy. Case histories report that the FTA may fluctuate between positive, negative, and mildly reactive in an individual with tertiary neurosyphilis, in individuals with syphilitic invasion of the kidneys, liver and lungs, and with ocular syphilis. (19-22, 26, 27, 30, 41-58)

In addition, a positive FTA with a history of syphilis does not exclude the possibility of a latent syphilis. That is, an individual with latent syphilis would be expected to have a positive FTA with or without a known history of syphilis. There is no test, therefore, to determine latent syphilis in an individual with a known history of syphilis. It is estimated that more than 60% of the gay community has a history of syphilis and 90% of those with AIDS have had one or more syphilitic infections. AIDS presentations following blood transfusions may be the result of syphilitic blood or plasma.

Sera from syphilitics is reported to exhibit immune suppression and to induce immune suppression both in vitro and in vivo. (61-66) Changes in both humoural immunity and cell mediated immunity are reported. (63-64) Plasma of patients with secondary syphilis suppressed the T cell response to Con A and has been reported to significantly supress the reactivity of normal lymphocytes to PHA stimulation. (65-66) If a blood or plasma recipient is receiving antibiotics or other immunosuppressive drugs, the combined immunosuppression of the syphilitic sera and chemical immunosuppression could induce an acquired immune deficiency syndrome. Screening of donors and serological testing may not be adequate for blood purity, particularly with seronegative syphilitic blood or immunosuppressive plasma from a syphilitic. The issue is further complicated by the lack of

general serological testing for latent syphilis of donor blood and by the possibilities of treponemes in chemically altered whole blood or in platelets surviving refrigeration. These are questions needing further investigation.

In view of a possible chemical suppression, a syphilitic immunosuppression, or a combined immunosuppression, how would we evaluate serologically a person infected with syphilis? Initially, we have recommended to our program participants that they obtain FTA and RPR serological tests for a baseline, and repeat the tests as any new symptoms arise.

We made this recommendation to them in early November 1985, and within a month, we had received the following reports regarding 16 of the 24 men with diagnoses of AIDS: one man had shown a positive Wassermann, three had positive MHAs with no previous history of syphilis, eight with known histories of syphilis were negative in their FTA-MHA antibody tests, and four with known histories of syphilis were FTA positive. Some of our clients' physicians, knowing that a history of syphilis exists and assuming that the FTA results would be positive, have refused to do the antibody test. Many of our program's participants, in addition, have volunteered that they had symptoms consistent with a primary syphilis episode prior to their AIDS diagnosis or consistent with the symptoms of secondary syphilis.

Men with a positive MHA or FTA without previous history or treatment for syphilis or negative MHA with a history of syphilis have agreed to undergo new biopsies for submission to the Center for Disease Control for darkfield and FA testing. Because darkfield examination may be difficult and a specific sample may not show active spirochetes, a second laboratory will also be undertaking darkfield and fluorescent antibody testing. TPI and repetition of serologies are also in progress.

CONCLUSIONS

Historically, the definition of acquired immune deficiency syndrome derives from known precursor factors: debilitation, malnourishment, drug immunosuppression, or chronic disease. This definition has been modified in the current "AIDS crisis" by the assumption that viral invasion has damaged the immune competency of otherwise healthy individuals. Analysis of a number of gay males with AIDS in San Francisco, however, has disclosed that excessive use of both prescriptive and recreational immunosuppressive drugs and chronic inflammations are universal precursor factors.

Drug induced immunosuppression and chronic inflammation are common factors in both American homosexual and native African populations diagnosed with AIDS. Both groups have epidemic syphilis. Investigation revealed links in the patterns of AIDS patients consistent with secondary and tertiary syphilis.

Immunosuppression of advanced syphilis and drug induced immunosuppression leads to false negative serology in antigen and antibody tests for syphilis. There is extensive reporting of symptomological and histopathological mimicking resulting in inaccurate diagnosis of secondary and tertiary syphilis.

Early antigen and antibody testing for syphilis of gay males with AIDS in San Francisco is revealing hitherto undiagnosed syphilis and abnormal antibody profiles.

It is our conclusion that the presentation of AIDS in Africa and the gay community reflects the common presence of chemical immunosuppression and epidemic syphilis, leading to the profound immunosuppression of acquired immune deficiency syndrome, AIDS.

REFERENCES

1. Dozier N, Ballentine R, Adams SC, Okafor KC. Acquired immune deficiency syndrome and the management of associated opportunistic infections. Drug Intel Clin Pharm 17(11): 798, 1983.

2. Cohen J. AIDS--a review. Br J Hos Med 31(4): 250, 1984.

3. Stahl RE, Friedman-Kien A, Zolla-Pazner S. AIDS: A medical conundrum. J Cut Path 10: 550, 1983.

4. Editorial. Kaposi's Sarcoma. Lancet 1: 300, 1973.

5. Siegal FP. Immune function and dysfunction in AIDS. Sem Oncol 11(1): 29, 1984.

6. Krieger T, Caceres CA. The Unnoticed Link in AIDS Cases. The Wall Street Journal, Oct. 24, 1985.

7. Brubaker ML. Syphilis. Chapters 16 and 40. Tropical Medicine, 5th ed. (Hunter, Swartzwelder, Clyde, eds) W.B. Saunders Co., Philadelphia, 1976.

8. Curran RC. Color Atlas of Histopathology. Revised. Harvey Miller-Oxford University Press, 1972.

9. Pathology, Vol. I and II. 7th ed. (WAD Anderson, JM Dissane, eds). C.V. Mosby Company. St. Louis, 1977.
   (a) Von Haam. Venereal Diseases and Spirochetal Infections, p. 437.
   (b) Allen AC, Skin, p. 1860.

10. Ackerman and del Regato's CANCER. 5th ed. (JA del Regato, HJ Spjut, eds) C.V. Mosby Company, St. Louis, p. 194, 1977.

11. Smego RA, Moreadith RW, Kleist PC, Granger DL. Secondary syphilis masquerading as AIDS in a young gay male. North Carolina Med J 45(4): 253, 1984.

12. McPhee, SJ. Secondary syphilis: Uncommon manifestations a common disease. West J Med 140(1): 35, 1984.

13. Chapel TA. Primary and secondary syphilis. CUTIS 33(1): 47, 1984.

14. Drusin LM. The diagnosis and treatment of infectious and latent syphilis. Med Clin North Am 56(5): 1161, 1972.

15. O'Regan S, Fong JSC, de Chadarevian JP, Rishikof JR, Drummond KN. Treponemal antigens in congenital and acquired syphilitic nephritis. Ann Inter Med 85: 325, 1976.

16. Walker PD, Deeves EC, Sahba G, Wallin JD, O'Neill WM. Rapidly progressive glomerulonephritis in a patient with syphilis. Am J Med 76: 1106, 1984.

17. Tourville DR, Byrd LH, Kim DU, Zajd D, Lee I, Reichman LB, Baskin S. Treponemal antigen in immunopathogenesis of syphilitic glomerulonephritis. Am J Pathol 82(3): 479, 1976.

18. Tight RR, Warner JF. Skeletal involvement in secondary syphilis detected by bone scanning. JAMA May 24: 235, 1976.

19. Nazemi MM, Musher DM, Schell RF, Milo S. Syphilitic proctitis in a homosexual. JAMA 231(4): 389, 1975.

20. Drusin LM, Singer C, Valenti AJ, Armstrong D. Infectious syphilis mimicking neoplastic disease. Arch Intern Med 137(2): 156, 1977.

21. Faris MR, Perry JJ, Westermeier TG, Redmond J. Rectal syphilis mimicking histiocytic lymphoma. Am J Clin Pathol 80: 719, 1983.

22. Parker JDJ. Uncommon complications of early syphilis, hepatitis, periostitis, iritis with papillitis, and meningitis. Br J Vener Dis 48: 32, 1972.

23. Carrera JL. A pathologic study of the lungs in one hundred and fifty-two autopsy cases of syphilis. Am J Syphilis 4(1): 1, 1920.

24. Howard CP. Pulmonary syphilis. Am J Syphilis 8(1): 1, 1924.

25. Hartung A, Freedman J. Pulmonary syphilis. JAMA 98(23): 1969, 1932.

26. Oslan HT, Chambers SO. Syphilitic pneumonia. Calif West Med 39(3): 185, 1933.

27. Morgan AD, Lloyd WE, Price-Thomas C. Tertiary syphilis of the lung and its diagnosis. Thorax 7: 125, 1952.

28. Schibli H, Harms M. Tumour-like pulmonary lesion in secondary syphilis. Br J Vener Dis 57: 367, 1981.

29. Coleman DL, McPhee SF, Ross TF, Naughton JL. Secondary syphilis with pulmonary involvement. West J Med 138(6): 875, 1983.

30. Willcox JR. An atypical case of secondary syphilis. Br J Vener Dis 57: 30, 1981.

31. Lejman K, Starzycki Z. Early varioliform syphilis. Br J Vener Dis 57: 25, 1981.

32. Beck MH, Hubbard HC, Dave VK, Haye KR. Secondary syphilis with framboesiform facial lesions. Br J Vener Dis 57: 103, 1981.

33. Lochner JC, Pomeranz JR. Lichenoid secondary syphilis. Arch Dermatol 109(1): 81, 1974.

34. Clark EG, Danbolt N. The Oslo study of the natural course of untreated syphilis. Med Clin North Am 48: 613, 1964.

35. Ross MW. Sexually transmitted diseases in homosexual men: A study of four societies. Br J Vener Dis 60: 52, 1984.

36. British Co-operative Clinical Group. Homosexuality and venereal disease in the United Kingdom. Br J Vener Dis 56: 6, 1980.

37. Owen WF. Sexually transmitted diseases and traumatic problems in homosexual men. Ann Intern Med 92: 805, 1980.

38. Bleeker A, Coutinho RA, Bakker-Kok J, Tio D, de Koning GAJ. Prevalence of syphilis and hepatitis B among homosexual men in two saunas in Amsterdam. Br J Vener Dis 57: 196, 1981.

39. Schroeter AL, Lucas JB, Price EV, Falcone VH. Treatment for early syphilis and reactivity of serologic tests. JAMA 221(5): 471, 1972.

40. Gillespie EJ, Brown BC. New laboratory methods in the diagnosis and management of syphilis. Med Clin North Am 48: 731, 1964.

41. Brown ST. Treatment of secondary syphilis. J Am Vener Dis Ass 3(2): 136, 1976.

42. Jaffe HW. Treatment of latent syphilis. J Am Vener Dis Ass 3(2): 143, 1976.

43. Olansky, S. Serodiagnosis of syphilis. Med Clin North Am 56(5): 1145, 1972.

44. Luger A, Schmidt B, Spendlingwimmer I, Horn F. Recent observations on the serology of syphilis. Br J Vener Dis 56: 12, 1980.

45. Masawe AEJ, Lomholt G, Aho K, Lassus A. Unusual behaviour of serological tests for syphilis in Ugandan Africans. Br J Vener Dis 48: 345, 1972.

46. Masawe AEJ. Serological tests for syphilis in Uganda. E Afr Med J 47(12): 673, 1970.

47. Osoba, AO: Sexually transmitted disease in tropical Africa: A review of the present situation. Br J Vener Dis 57: 89, 1981.

48. Collart P, Franceschini P, Poitevin M, Dunoyer F, Dunoyer M. Modified method of filtering cerebrospinal fluid and aqueous humour for the detection of treponemes; Proof of the persistence of their vitality in rabbits. Br J Vener Dis 50: 251, 1974.

49. Smith JL, Israel CW. The presence of spirochetes in late seronegative syphilis. JAMA 199(13): 126, 1967.

50. Sowmini CN. Clinical progression of ocular syphilis and neurosyphilis despite treatment with massive doses of penicillin. Failure to demonstrate treponemes in affected tissues. Br J Vener Dis 47: 348, 1971.

51. Collart P, Pechere JC, Franceschini P, Dunoyer P. Persisting virulence of T. pallidum after incubation with penicillin in Nelson-Mayer medium. Br J Vener Dis 48: 29, 1972.

52. Yogeswari L, Chacko CW. Persistence of T. pallidum and its significance in penicillin-treated seropositive late syphilis. Br J Vener Dis 47: 339, 1971.

53. Lauderdale V, Goldman JN. Serial ultrathin sectioning demonstrating the intracellularity of T. pallidum. Br J Vener Dis 48: 87, 1972.

54. Yobs AR, Rockwell DH, Clark JW. Treponemal survival in humans after penicillin therapy. Br J Vener Dis 40: 248, 1964.

55. Rice NSC, Dunlop EMC, Jones BR, Hare MJ, King AJ, Rodin P, Mushin A, Wilkinson AE. Demonstration of treponeme-like forms in cases of treated and untreated late syphilis and of treated early syphilis. Br J Vener Dis 46: 1, 1970.

56. Smith JL. Spirochetes in late seronegative syphilis despite penicillin therapy. Med Times 96(6): 611, 1968.

57. Collart P, Poitevin M. Is penicillin therapy always infallible in syphilis? J Clin Neuro-ophthalmol 2: 77, 1982.

58. Hollander DH, Turner TB, Nell EE. The effect of long continued subcurative doses of penicillin during the incubation period of experimental syphilis. Bull Johns Hopk Hosp 90: 105, 1952.

59. Collart P, Franceschini P, Durel P. Experimental rabbit syphilis. Br J Vener Dis 47: 389, 1971.

60. Thompson JJ, Mangi RJ, Lee R, Dwyer JM. Immunoregulatory properties of serum from patients with different stages of syphilis. Br J Vener Dis 56: 210, 1980.

61. Dwyer JM, Kantor FS. In vivo suppression of delayed hypersensitivity: Prolongation of desensitization in guinea pigs. J Exp Med 142: 588, 1975.

62. Bos JD, Hamerlinck F, Cormane RH. Antitreponemal IgE in early syphilis. Br J Vener Dis 56: 20, 1980.

63. Hrncir Z, Kraus Z, Tichy M. Non-specific humoural immunity response in latent and tertiary syphilis. Brit J Vener Dis 48: 108, 1972.

64. Pavia CS, Folds JD, Baseman JB. Cell-mediated immunity during syphilis. Brit J Vener Dis 54: 144, 1978.

65. Jensen JR, From E. Alterations in T lymphocytes and T-lymphocyte subpopulations in patients with syphilis. Brit J Vener Dis 58: 18, 1982.

66. From E, Thestrup-Pedersen K, Thulin H. Reactivity of lymphocytes from patients with syphilis toward T. pallidum antigen in the leucocyte migration and lymphocyte transformation tests. Brit J Vener Dis 56: 224, 1976.

67. Jeerapaet P, Ackerman AB. Histologic patterns of secondary syphilis. Arch Dermatol 107(3): 373, 1973.

68. Wolman M, Izak G, Freund E, Shamir Z. Studies on interstitial giant cell pneumonia. Am J Dis Child 83(5): 573, 1952.

69. Pavlica F. The first observation of congenital pneumocystic pneumonia in a fully developed stillborn child. Ann Paediat 198: 177, 1962.

70. Gormsen H. On interstitial plasma cell pneumonia in infants. ACTA Pediat 39: 291, 1950.

71. Perera DR, Western KA, Johnson HD, Johnson WW, Schultz MG, Akers PV. Pneumocystis carinii pneumonia in a hospital for children. JAMA 214(6): 1074, 1970.

72. Russell GR, Brown WE, Betts WA. Primary atypical pneumonia in childhood. S Med J 45(10): 906, 1952.

73. Nowak J. Late pulmonary changes in the course of infection with pneumocystis carinii. ACTA Med Pol 7(1): 23, 1966.

74. Robertson PW, Morle KDF. An explanation of the "primary atypical pneumonia" syndrome. Br Med J 2(10): 994, 1951.

75. Randolph MF. Primary atypical pneumonia in children. Conn State Med J 14: 19, 1950.

76. Troen P. Explosive outbreak of an atypical pneumonia. Arch Intern Med 89: 258, 1952.

77. Myers BD, Kessler E, Levi J, Pick A, Rosenfeld JB, Tikvah P. Kaposi's sarcoma in kidney transplant recipients. Arch Intern Med 133(2): 307, 1974.

78. Reynolds WA, Winkelmann RK, Soule EH. Kaposi's Sarcoma: A clinicopathologic study with particular reference to its relationship to the reticuloendothelial system. Medicine 44(5): 419, 1965.

79. Master SP, Taylor JF, Kyalwazi SK, Ziegler JL. Immunological studies in Kaposi's sarcoma in Uganda. Br Med J 1(3): 600, 1970.

80. Haim S, Shafrir A, Better OS, Robinson E, Chaimowitz C, Erlik D. Kaposi's sarcoma in association with immunosuppressive therapy. Isr J Med Sci 8(12): 1993, 1973.

81. Kahn LB, Gordon W. Sarcoid-like granulomas in secondary syphilis. Arch Path 92(11): 334, 1971.